ingredients for the constructive development of thought and action in introducing new technologies. This is particularly the case for genetic tests used for prenatal diagnosis and selective termination of pregnancies.

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Reply to Michie and Marteau

To the Editor:

Michie and Marteau (1999 [in this issue]) make some valid points in relation to our article on attitudes toward genetic testing for deafness (Middleton et al. 1998). However, they also make some criticisms that we would like to take the opportunity to answer. Michie and Marteau point out that the study sample is likely to be unrepresentative of deaf people. It was acknowledged in our article that the study sample was biased. In fact, a culturally biased sample was chosen deliberately, since it was cultural attitudes that were of interest. Another criticism in their letter is that "participants completed the questionnaires in a highly unusual social context." Again, it was acknowledged in our article that the "responses may have been influenced by the context within which the questionnaire was distributed," and "social desirability bias" was cited as a possible confounding factor. The article was the result of a pilot study that, together with other pilot work, contributed to the design of a larger study that has ascertained the attitudes of 1,600 deaf, hard-of-hearing, or deafened adults and

hearing individuals with a family history of deafness. From the results of this larger study, it will be possible to see how the sample used in the article fits into a more general sample from the deaf community. Preliminary analysis of the results from the larger study shows that, although the attitudes expressed in our article are more negative than those based on the larger sample, the trends are the same. The results of this larger study are in the process of being written up for publication.

Michie and Marteau also say that we proposed that specialized counselors should be required for every disease and disability. This was not what we suggested. We advocated that language and cultural barriers could be kept to a minimum by the use of deaf genetic counselors to see deaf clients, in the same way that Asian counselors might counsel Asian clients in their own language, recognizing transcultural aspects in the genetic counseling process, rather than just the use of interpreters in this situation. We actually emphasized that it is unrealistic to suggest that only disabled people could counsel disabled clients.

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Using Exact *P* Values to Compare the Power between the Reconstruction-Combined Transmission/ Disequilibrium Test and the Sib Transmission/ Disequilibrium Test

To the Editor:

In a recent letter in the *Journal,* Laird et al. (1998) pointed out that Spielman and Ewens's (1998) sib transmission/disequilibrium test (S-TDT) is identical to a Mantel-Haenszel test of trend. As noted by Laird et al., it is possible by this identity to use commercial software such as StatXact to calculate exact *P* values for the S-TDT. The superiority of exact *P* values over asymptotic *P* values is evident, since it is well known (e.g., see Elston 1998) that *P* values obtained on the basis of theoretical large-sample approximations can be quite unreliable if they are much smaller than .05. An example of the need of small *P* values is the association scan proposed by Risch and Merikangas (1996), which requires that *P* values $< 5 \times 10^{-8}$ be observed in order for significance to be declared.

It does not seem to be generally known that the calculation of exact *P* values for the S-TDT does not require sophisticated algorithms at all. To the contrary, it is easily incorporated into any computer program. In essence, the test statistic of the S-TDT is the total number T of alleles A (i.e., the allele of interest) in affected children in the whole sample. The null distribution of T is the convolution of all null distributions for T_i, where T_i denotes the number of alleles A in family i. The null distribution of T_i, conditional on the observed numbers n_{ai} of affected children and n_{ui} of unaffected children and on the observed marker-genotype distribution in family i, is easily calculated from a hypergeometric distribution and is concentrated on, at most, $2n_{ai} + 1$ different values. The numerical calculation of the convolution of such distributions concentrated on a small part of the natural numbers is quite feasible, at least for sample sizes typically occurring in practice (see below). The situation is very similar for the reconstruction-combined transmission/disequilibrium test (RC-TDT [Knapp 1999]), which employs reconstruction of missing parental genotypes to enhance the power of the S-TDT. This test, which does not seem to be identical to any standard statistical procedure and, therefore, requires special software for its application, also allows the calculation of exact *P* values.

I have written an SAS (SAS Institute 1990) macro that calculates exact *P* values for the S-TDT and RC-TDT, as well as *P* values based on z scores (with and without continuity correction). In order to give an impression of the time performance of this program, it was applied to allele M7 of marker D5G23 in Genetic Analysis Workshop 9 data (Hodge 1995). When all parental genotypes in these families are assumed to be unknown, 107 families remain that can be analyzed with the S-TDT and the RC-TDT. The program required less than 3 CPU-seconds for this analysis, on a low-end IBM RS6000 workstation. If each family is multiplied 10-fold (i.e., resulting in a data set of 1,070 families, which is more than the sample sizes usually occurring in practice), the SAS macro required 24 CPU-seconds.

The implementation of the RC-TDT in this macro differs, in two points, from the description given by Knapp (1999) and from the program formerly used to compare the power of the RC-TDT versus that of the